REMARKS/ARGUMENTS

The Pending Claims

Claims 1, 7-15, and 17-26 are pending. Pursuant to a restriction requirement, claims 7-14 and claims 21-26 have been withdrawn. Claims 1, 15, and 17-20 currently are subject to examination.

The Amendments to the Claims

Claim 1 has been amended to incorporate, in part, the subject matter of former claim 16, which has been cancelled. Claim 1 also has been amended to recite assaying the copy number or the expression level of SEQ ID NO: 1, and to recite that the presence of NeuroAIDS in the mammal is indicated by expression of SEQ ID NO: 1 at levels at least 2.5 times greater than expression of SEQ ID NO:1 in a control sample. Claims 15 and 20 have been amended to recite that the method comprises assaying the expression level of SEQ ID NO: 1. These amendments are supported by the original claims and the specification at, e.g., paragraphs 0010, 0019, and 0073. Accordingly, no new matter has been added by way of these amendments.

Discussion of Rejections Under 35 U.S.C. 112, First Paragraph

Claims 1 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement and written description. These rejections are traversed for the reasons set forth below.

A. Enablement

The Office Action alleges that claims 1 and 15-20 are not enabled in several respects: (1) the specification does not disclose any working examples demonstrating diagnosis of a neurodegenerative disease based on detection of overexpression of Cripto-1, (2) the specification does not disclose any studies performed in humans, (3) correlating altered gene expression to phenotype is unpredictable, and (4) simian HIV (SHIV) is not representative of "any" neurodegenerative disease.

Claim 1, as amended, is directed to a method of detecting NeuroAIDS in a mammal comprising assaying the copy number of SEQ ID NO: 1 or the expression level of SEQ ID NO: 1 in the central nervous system of the mammal, wherein the presence of NeuroAIDS in the mammal is indicated by (a) an amplification of SEQ ID NO: 1 or (b) expression of SEQ ID NO: 1 at levels at least 2.5 times greater than expression of SEQ ID NO:1 in a control sample.

Example 2 of the present patent application discloses that the Cripto-1 gene is overexpressed in a macaque model of NeuroAIDS, and thus, the Cripto-1 gene can be used as a diagnostic marker for NeuroAIDS. While the Office Action raises general concerns regarding the sample size tested and the purported unpredictability associated with measuring and correlating altered gene expression to a particular phenotype, the examples cited by the Office Action do not provide specific evidence to question the ability to detect NeuroAIDS by assaying Cripto-1 gene copy number or expression levels. The Office is reminded that the applicant does not have to prove that a correlation exists between a particular activity and an asserted use of a compound as a matter of statistical certainty. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. *In re Brana*, 51 F.3d. 1560, 1566, 1541, 34 U.S.P.Q. 2d. 1436, 1441 (Fed. Cir. 1995); *Nelson v. Bowler*, 626 F.2d 853, 857, 206 U.S.P.Q. 881, 884 (C.C.P.A. 1980); *Cross v. Izuka*, 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. 885 (C.C.P.A. 1980); *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. 881 (C.C.P.A. 1980).

The simian immunodeficiency virus (SIV) and SHIV macaque employed in the examples are well-established animal models of HIV infection in humans and were considered to be so at the time the subject application was filed (see, e.g., Liu et al., *Virology*, *260*: 295-307 (1999), McCormick et al., *Virology*, *272*: 112-126 (2000), Raghavan et al., *Brain Pathol.*, *7*: 851-861 (1997), Nehete et al., *Vaccine*, *20*(5-6): 813-825 (2001), Weber et al., *AIDS*, *15*(12): 1563-1568 (2001), and Harouse et al., *J. Virol.*, *75*(4): 1990-1995 (2001)). Moreover, SIV-infected macaque models for HIV-induced neurological disease were known in the art at the time the present application was filed (see, e.g., Sopper et al., *J. Neural Transm.*, *109* (506): 747-766 (2002), Zink et al., *NeuroAIDS*, *3*, Issue 5 (2000), and Klein et al., *J. Immunol.*, *163*: 1636-1646 (1999)). Accordingly, the experimental results for the SHIV

macaque model disclosed in the instant application are readily translatable to HIV infection in humans.

In view of the amendments to the claims and the foregoing arguments, the specification enables the subject matter defined by claim 1, and claims 15 and 17-20 depending therefrom. Accordingly, Applicants request withdrawal of the enablement rejection.

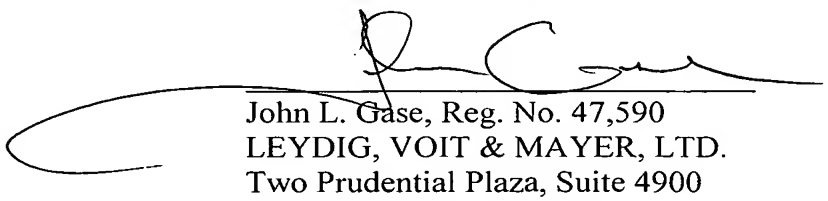
B. Written Description

The Office Action contends that claims 1 and 15-20 lack adequate written description because the specification does not disclose a representative number of species of the Cripto-1 gene, nor does it disclose any structural requirements for a Cripto-1 gene product. While Applicants disagree with this rejection, the claims have been amended to recite a specific Cripto-1 nucleic acid sequence (i.e., SEQ ID NO: 1). Accordingly, the written description rejection is rendered moot by these amendments and should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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